

CLAIMS

1. A polypeptide, which polypeptide:

- (i) comprises the amino acid sequence as recited in SEQ ID NO:2, or
- (ii) is a fragment thereof having 5-HT3 protein function or having an antigenic determinant in common with the polypeptide of (i); or
- (iii) is a functional equivalent of (i) or (ii).

2. A polypeptide or a functional equivalent which is a 5-HT3 receptor subunit.

3. A polypeptide or a functional equivalent according to claim 2 which forms a homopentamer.

10 4. A polypeptide or a functional equivalent according to claim 2 which forms a heteropentamer.

5. A polypeptide or a functional equivalent according to claim 4, wherein the heteropentamer includes subunits from other ligand-gated ion channels.

15 6. A polypeptide or a functional equivalent according to claim 5, wherein the heteropentamer includes subunits from other 5-HT3 receptors.

7. A polypeptide which is a functional equivalent according to claim 1(iii) or claims 2 to 6, is homologous to the amino acid sequence as recited in SEQ ID NO:2, and has 5-HT3 receptor activity.

20 8. A fragment or functional equivalent according to any of claims 1-7, which has greater than 95% sequence identity with the amino acid sequence recited SEQ ID NO:2, or with active fragments thereof, preferably greater than 95%, 98% or 99% sequence identity.

25 9. A functional equivalent according to any one of claims 1-8, which exhibits significant structural homology with a polypeptide having the amino acid sequence given in SEQ ID NO:2.

10. A fragment as recited in claim 1 or claim 8 having an antigenic determinant in common with the polypeptide of claim 1(i), which consists of 7 or more (for example,

8, 10, 12, 14, 16, 18, 20 or more) amino acid residues from the sequence SEQ ID NO:2.

11. A fragment according to claim 10 comprising amino acid residues 24 to 421 of SEQ ID NO:2.

5 12. A fragment according to claim 10 comprising amino acid residues 24 to 229 of SEQ ID NO:2.

13. A fusion protein comprising:

- 10 1) a ligand binding domain derived from a polypeptide according to any one of claims 1 to 8 and a transmembrane domain derived from another member of the 5-HT3 receptor group; or
- 2) a transmembrane domain derived from a polypeptide according to any one of claims 1 to 8 and a ligand binding domain derived from another member of the 5-HT3 receptor group.

14. A fusion protein according to claim 13, part 1) comprising the amino acid sequence 15 as recited in SEQ ID NO:23 or a fusion protein according to claim 13, part 2) comprising the amino acid sequence as recited in SEQ ID NO:24.

15. A purified nucleic acid molecule which encodes a polypeptide according to any one of the preceding claims.

16. A purified nucleic acid molecule according to claim 15, which has the nucleic acid 20 sequence as recited in SEQ ID NO:1, or is a redundant equivalent or fragment thereof.

17. A purified nucleic acid molecule which hybridises under high stringency conditions with a nucleic acid molecule according to claim 15 or claim 16.

18. A vector comprising a nucleic acid molecule as recited in any one of claims 15-17.

25 19. A host cell transformed with a vector according to claim 18.

20. A ligand which binds specifically to, and which preferably modulates the activity of, a polypeptide according to any one of claims 1-14 as a member of the 5-HT3 receptor group.

21. A ligand according to claim 20 which binds specifically to the ligand binding domain or the pore forming domain of a polypeptide according to any one of claims 1- 14
22. A ligand according to claim 21, which is an antibody.
23. A compound that either increases or decreases the level of expression or activity of a
5 polypeptide according to any one of claims 1-14.
24. A compound according to claim 23 that binds to a polypeptide according to any one of claims 1-15 without inducing any of the biological effects of the polypeptide.
25. A compound according to claim 24, which is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic.
- 10 26. A polypeptide according to any one of claims 1-14, a nucleic acid molecule according to any one of claims 15-17, a vector according to claim 18, a host cell according to claim 19, a ligand according to any one of claims 20 to 22, or a compound according to any one of claims 23-25, for use in therapy or diagnosis of disease.
27. A method of diagnosing a disease in a patient, comprising assessing the level of
15 expression of a natural gene encoding a polypeptide according to any one of claims 1-14, or assessing the activity of a polypeptide according to any one of claims 1-14, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease.
28. A method according to claim 27 that is carried out *in vitro*.
- 20 29. A method according to claim 27 or claim 28, which comprises the steps of: (a) contacting a ligand according to any one of claims 20 to 22 with a biological sample under conditions suitable for the formation of a ligand-polypeptide complex; and (b) detecting said complex.
30. A method according to claim 27 or claim 28, comprising the steps of:
25 a) contacting a sample of tissue from the patient with a nucleic acid probe under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 15-17 and the probe;
b) contacting a control sample with said probe under the same conditions used in step a);

• and

c) detecting the presence of hybrid complexes in said samples; wherein detection of levels of the hybrid complex in the patient sample that differ from levels of the hybrid complex in the control sample is indicative of disease.

5 31. A method according to claim 27 or claim 28, comprising:

a) contacting a sample of nucleic acid from tissue of the patient with a nucleic acid primer under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 15-17 and the primer;

b) contacting a control sample with said primer under the same conditions used in step a);

10 and

c) amplifying the sampled nucleic acid; and

d) detecting the level of amplified nucleic acid from both patient and control samples; wherein detection of levels of the amplified nucleic acid in the patient sample that differ significantly from levels of the amplified nucleic acid in the control sample is indicative of disease.

15 32. A method according to claim 27 or claim 28 comprising:

a) obtaining a tissue sample from a patient being tested for disease;

b) isolating a nucleic acid molecule according to any one of claims 15-17 from said tissue sample; and

20 c) diagnosing the patient for disease by detecting the presence of a mutation which is associated with disease in the nucleic acid molecule as an indication of the disease.

33. The method of claim 32, further comprising amplifying the nucleic acid molecule to form an amplified product and detecting the presence or absence of a mutation in the amplified product.

25 34. The method of either claim 32 or 33, wherein the presence or absence of the mutation in the patient is detected by contacting said nucleic acid molecule with a nucleic acid probe that hybridises to said nucleic acid molecule under stringent conditions to form a hybrid double-stranded molecule, the hybrid double-stranded molecule having an

unhybridised portion of the nucleic acid probe strand at any portion corresponding to a mutation associated with disease; and detecting the presence or absence of an unhybridised portion of the probe strand as an indication of the presence or absence of a disease-associated mutation.

5 35. A method according to any one of claims 27-34, wherein said disease includes, but is not limited to, nausea, vomiting, pain, eating disorders, alcoholism, psychosis, side effects of various anticancer therapies, irritable bowel syndrome, gastrointestinal related disorders, Alzheimer's disease, Parkinson's disease, Huntingtons Chorea, cognitive disorders, behavioral disorders and phobias such as anxiety related illnesses and addiction, obsessive compulsive behavior, memory and learning disorders, depression and panic disorders, asthma, inflammation, sexual dysfunction, disorders of the neuroendocrine and cardiovascular systems.

10 36. A method according to any one of claims 27-34, wherein said disease includes diseases associated T cells such as inflammatory bowel diseases (including Crohns disease and ulcerative colitis), multiple sclerosis, psoriasis, rheumatoid arthritis, thrombocytopenia, type I diabetes mellitus, asthma, atopic dermatitis, atopic rhinitis and conjunctivitis, diseases associated with T cell proliferation such as leukaemias, diseases associated with T-cell depletion such as HIV infection, chemotherapy and radiotherapy, and diseases where regulation of T cell activation is required, such as cancers, viral infections, bacterial infections (including tuberculosis) and fungal infections.

15 37. Use of a polypeptide according to any one of claims 1-14 as a member of the 5HT-3 receptor group.

20 38. A pharmaceutical composition comprising a polypeptide according to any one of claims 1-14, a nucleic acid molecule according to any one of claims 15-17, a vector according to claim 18, a host cell according to claim 19, a ligand according to any of claims 20 to 22, or a compound according to any one of claims 23-25.

25 39. A vaccine composition comprising a polypeptide according to any one of claims 1-14 or a nucleic acid molecule according to any one of claims 15-17.

40. A polypeptide according to any one of claims 1-14, a nucleic acid molecule according to any one of claims 15-17, a vector according to claim 18, a host cell according to claim 19, a ligand according to any one of claims 20 to 22, a compound according to any one of claims 23-25, or a pharmaceutical composition according to claim 38, for use in the manufacture of a medicament for the treatment of certain disease including, but not limited to, nausea, vomiting, pain, eating disorders, alcoholism, psychosis, side effects of various anticancer therapies, irritable bowel syndrome, gastrointestinal related disorders, Alzheimer's disease, Parkinson's disease, Huntington's disease, cognitive disorders, behavioural disorders and phobias such as anxiety related illnesses and addiction, obsessive compulsive behaviour, memory and learning disorders, depression and panic disorders, asthma, inflammation, sexual dysfunction, disorders of the neuroendocrine and cardiovascular systems.

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41. A polypeptide according to any one of claims 1-14, a nucleic acid molecule according to any one of claims 15-17, a vector according to claim 18, a host cell according to claim 19, a ligand according to any one of claims 20 to 22, a compound according to any one of claims 23-25, or a pharmaceutical composition according to claim 38, for use in the manufacture of a medicament for the treatment of diseases associated T cells such as inflammatory bowel diseases (including Crohns disease and ulcerative colitis), multiple sclerosis, psoriasis, rheumatoid arthritis, thrombocytopenia type I diabetes mellitus, asthma, atopic dermatitis, atopic rhinitis and conjunctivitis, diseases associated with T cell proliferation such as leukaemias, diseases associated with T-cell depletion such as HIV infection, chemotherapy and radiotherapy, and diseases where regulation of T cell activation is required, such as cancers, viral infections, bacterial infections (including tuberculosis) and fungal infections.

42. A method of treating a disease in a patient, comprising administering to the patient a polypeptide according to any one of claims 1-14, a nucleic acid molecule according to any one of claims 15-17, a vector according to claim 18, a host cell according to claim 19, a ligand according to any one of claims 20 to 22, a compound according to any one of claims 23-25, or a pharmaceutical composition according to claim 38.

43. A method according to claim 42, wherein, for diseases in which the expression of the

natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an agonist.

- 5 44. A method according to claim 42, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an antagonist.
- 10 45. A method of monitoring the therapeutic treatment of disease in a patient, comprising monitoring over a period of time the level of expression or activity of a polypeptide according to any one of claims 1-14, or the level of expression of a nucleic acid molecule according to any one of claims 15-17 in tissue from said patient, wherein altering said level of expression or activity over the period of time towards a control level is indicative of regression of said disease.
- 15 46. A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a polypeptide according to any one of claims 1-14, or a nucleic acid molecule according to any one of claims 15-17 with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said nucleic acid molecule or polypeptide.
- 20 47. A kit useful for diagnosing disease comprising a first container containing a nucleic acid probe that hybridises under stringent conditions with a nucleic acid molecule according to any one of claims 15-17; a second container containing primers useful for amplifying said nucleic acid molecule; and instructions for using the probe and primers for facilitating the diagnosis of disease.
- 25 48. The kit of claim 47, further comprising a third container holding an agent for digesting unhybridised RNA.
49. A kit comprising an array of nucleic acid molecules, at least one of which is a nucleic